REMARKS

Claims 72, and 74 - 91 are pending in the current application. Claim 73 was previously cancelled.

Rejections under 35 USC §§101 & 112

All prior rejections under 35 USC §§101 and 112 have now been withdrawn by the Examiner.

Rejections under 35 USC §102& 103

All prior rejections under 35 USC §102 have now been withdrawn by the Examiner. Additionally, the rejections under 35 USC §103 based on Foldvari et al. in view of Mackles and Foldvari et al. in view of Bott have also been withdrawn. However, the Examiner has instituted new grounds of rejection under §103.

Rejection of Claims 72, 74-79, 81, 83-84, and 87-88 under 35 USC §103 as unpatentable over Foldvari et al. in view of Kosal

The Examiner argued (Office Action, page 4) that Foldvari discloses a composition that includes an oil-in-water (O/W) emulsion for transdermal administration and also teaches a transdermal device for administration of the composition. The Examiner conceded that Foldvari does not disclose a silicone component contained within the emulsion. The Examiner cited Kosal as a teaching of a pressure sensitive adhesive emulsion where the silicone phase is emulsified in a continuous water phase. The Examiner concluded that it would have been obvious to combine the teachings of Foldvari with "the silicone pressure sensitive adhesive of Kosal" to obtain the benefit of "performance properties such as controlled tack."

With specific regard to claim 72, the Examiner stated that Foldvari teaches a composition comprised of an oil-in-water emulsion that additionally includes an immunogen (i.e. protein) incorporated into the emulsion. The Examiner further stated that Foldvari discloses a hydrophilic solvent (i.e. being substantially free of lipophilic solvent). The Examiner argued that although Foldvari does not disclose the emulsion as being formed by mechanical inversion, the process by which the composition is made is irrelevant where the composition disclosed by the

prior art is structurally equivalent to the composition that the applicant is claiming. Kosal was said to teach the feature of a silicone phase emulsified in a continuous water phase.

As previously explained by applicants, the silicone component disclosed in Foldvari is an adhesive layer 50 made from a pharmaceutically acceptable pressure sensitive adhesive, such as polydimethylsiloxane. (*See* Column 9, lines 49-53). The adhesive layer 50 is a means by which a transdermal device is affixed to the skin. (*See* Column 9, lines 49-50). However, the adhesive layer is not located within the hydrophobic phase of the emulsion as recited in claim 72. Rather, the adhesive layer is separate from the emulsion component of the biphasic lipid vesicles disclosed in Foldvari.

Specifically, the biphasic lipid vesicles disclosed in Foldvari include an oil-in-water emulsion 22, 24, 26 in the central core compartment of the lipid vesicle and in the aqueous space separating the lipid bilayers 12, 14. (*See* FIG. 1 and Column 5, lines 49-52). The transdermal device 40 includes a reservoir 42 adapted to retain during storage and release in operation lipid vesicles containing an entrapped antigen. (*See* Column 9, lines 9-10 and 15-16). The reservoir 42 is defined by an impermeable backing layer 44 and a membrane 46. (*See* FIG. 3A and Column 9, lines 16-17). The adhesive layer 50, made from a pharmaceutically acceptable pressure sensitive adhesive, is a means for affixing the device to the skin of the subject. (*See* FIG. 3A).

Thus, in Foldvari, the adhesive layer 50 is separated from the reservoir 42 adapted to retain lipid vesicles, where the emulsion is located. Consequently the pressure sensitive adhesive, such as polydimethylsiloxane, is not located within the hydrophobic component of the emulsion, as recited in amended claim 72. As now conceded by the Examiner, Foldvari fails to teach or suggest "a hydrophobic phase comprising a silicone component " as recited in amended claim 72.

The Examiner now cites Kosal who teaches a pressure sensitive silicone adhesive formulation. The Examiner refers to column 5 of Kosal where Kosal teaches that the pressure sensitive adhesive can have many uses including adhesive coatings for paper labels and sealing strips, in eye cosmetics, and in "medical applications such as transdermal drug delivery patches." Foldvari also teaches a transdermal delivery system. The Examiner proposes to combine the teachings of Kosal with Foldvari to arrive at the claimed invention. However, even if combined in the manner proposed, the claimed invention will not result. As discussed above, Foldvari uses

a pressure sensitive adhesive to adhere the transdermal delivery device to the skin of a patient. As shown for example in Fig. 3A of Foldvari, the active immunogen is contained in Foldvari's lipid vesicles in reservoir 42. The active immunogen passes through membrane 46 and adhesive layer 50 to reach the skin. Thus, if one skilled in the art were to combine the teachings of Kosal with Foldvari, one would substitute the adhesive of Kosal for the adhesive 50 of Foldvari to, as the Examiner speculates, provide "advantageous performance properties such as controlled tack." However, the resulting Foldvari/Kosal transdermal patch would still not meet the claims. Specifically, with respect to independent claim 72, the modified Foldvari/Kosal patch would still not include a hydrophobic phase comprising a silicone component. Rather, the hydrophobic phase in Foldvari/Kosal would comprise the same oils such as olive oil (col. 11, line 42 and Example 1). Nowhere in either Foldvari or Kosal is the slightest hint or suggestion to substitute a pressure sensitive silicone adhesive for the olive oil phase of Foldvari. As the combination of reference teachings fail to meet claim 72, as well as claims 74-79, 81, 83-84, and 87-88 which depend directly or indirectly therefrom, applicants submit that the rejection fails and should be withdrawn.

Rejection of Claim 89 under 35 USC §103(a) as unpatentable over Foldvari in view of Kosal and Mackles et al.

The Examiner repeated the prior rejection of claim 89, but has now added the newly-cited Kosal. Claim 89 depends indirectly from claim 72. As discussed above, even if Kosal's teachings were to be combined with Foldvari, the claimed invention would not be met. Mackles fails to make up for the deficiencies noted in the combination of Foldvari and Kosal. Accordingly, applicants submit that claim 89 is patentable for at least the same reasons that claim 72 is patentable.

Further, claim 89 recites "[a] controlled release composition as set forth in claim 87 wherein said controlled-release layer is dry in said dressing such that said controlled-release layer is free of water after said controlled-release layer is formed by said controlled-release composition." The controlled release layer recited in claim 87 is "formed from said controlled release composition of claim 72." Applicants submit that the Examiner is incorrect in her assertion that Mackles teaches anhydrous topical bases that function as delivery systems for medications further in the form of an oil-in-water emulsion.

While Mackles does disclose the use of anhydrous compositions suitable for topical application, Mackles does not teach or suggest anhydrous topical bases that function as delivery systems for medications in the form of an oil-in-water emulsion. (*See* Column 1, lines 6-7). Conversely, Mackles distinguishes the disclosed anhydrous composition from efforts to improve dermatological vehicles including oil-in-water emulsion systems in which the oil was dispersed in at least 50% water to form a lotion or a cream. (*See* Column 1, lines 43-47). Additionally, Mackles further distinguishes anhydrous topical bases from the previous systems stating that they suffer from several negatives. (*See* Column 1, lines 53-55). Moreover, Mackles teaches away from the use of an emulsion disclosing that "emulsions are inherently unstable systems that separate in time." (*See* Column 2, lines 3-4). Thus, contrary to the Examiner's assertions, it would not have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Foldvari with the anhydrous feature of the topical composition disclosed in Mackles where Mackles discloses the instability of emulsions.

While Mackles discloses that water sometimes results in active ingredient instability, Mackles teaches away from the use of an emulsion, teaching that emulsions are inherently unstable. Thus, one of ordinary skill in the art would not be led to use an emulsion in a "controlled release layer free of water" as recited in claim 89. Applicants submit that claim 89 is patentable over the combination of reference teachings.

Rejection of Claims 80, 82 and 85-86 under 35 USC §103(a) as unpatentable over Foldvari in view of Kosal taken further with Bott et al. and Kanios et al

The Examiner rejected claims 80, 82, and 85-86 under 35 USC §103(a) as being unpatentable over Foldvari, Bott, and Kanios as before, but now with the use of newly-cited Kosal. Claims 80, 82, and 85-86 depend indirectly from claim 72. As discussed above, even if Kosal's teachings were to be combined with Foldvari, the claimed invention would not be met. Bott and Kanios fail to make up for the deficiencies noted in the combination of Foldvari and Kosal. Accordingly, applicants submit that claims 80, 82, and 85-86 are patentable for at least the same reasons that claim 72 is patentable.

No grounds of rejection were stated with respect to Claims 90-91.

In the Office Action, the Examiner failed to state any grounds of rejection for claims 90 and 91. At page 2 of the Action, the Examiner withdrew the previous rejection of claim 90 under §§101 and 112. As claims 90 and 91 were not rejected on any basis, applicants submit that those claims are patentable as well.

Conclusion

It is believed that the above represents a complete response to the rejection set forth in the Official Action, and places the present application in condition for allowance. Reconsideration and an early allowance are requested.

Respectfully submitted,
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